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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/463,851	06/05/00	ACHENBACH H	A32964PCT/U

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EXAMINER	
PATTEN, P	
ART UNIT	**PAPER NUMBER**
1651	7

DATE MAILED: 01/04/01

Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/463,851	Applicant(s) Achenbach, H.
	Examiner Patricia Patten	Group Art Unit 1651

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *53-71* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *53-71* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 6

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Priority

This application filed lacks the necessary reference to the prior application. A statement reading "This is a 371 of PCT/GB98/02317 , filed _____." should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of all nonprovisional parent applications referenced should be included.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 53-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting fungal growth *in-vitro* or inhibiting mutagenesis in a microorganism via administration of an organic solvent extract of *Aristolochia taliscana*, does not reasonably provide enablement for a method for inhibiting mutagenesis, inhibiting fungal growth or inhibiting inflammation in an organism . The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Inventions targeted for human therapy bear a heavy responsibility to provide supporting evidence because of the unpredictability in biological responses to therapeutic treatments. The standard of enablement is higher for such inventions because effective treatments for disease

conditions are relatively rare, and may be unbelievable in the absence of strong supporting evidence. Claims drawn to pharmaceutically acceptable compositions and to methods of administering compounds to humans generally require supporting evidence because of the unpredictability in biological responses to therapeutic treatments.

In the instant case, although Applicants have shown that the benzene extract of *Aristolochia taliscana* may have anti-fungal properties as well as anti-mutagenic properties *in-vitro*, does not provide any indication that the extract would be beneficial for *in-vivo* use.

The art of microbial control of fungal infections in mammals is unpredictable. The instant specification as filed has not provided adequate information regarding any effective treatments of fungal infections. Applicants have provided data which clearly demonstrates the effectiveness of the composition of the instant invention *in vitro*, however, successful *in vitro* data does not necessarily mean that the composition of the present invention will work *in vivo* considering the unpredictability of the art, and the lack of guidance in the present disclosure.

Wickware (1997) pointed out that there are numerous obstacles regarding successful fungal treatments such as the fungi's resistance to certain anti-fungal drugs and the interference of the bodies own immune system in drug treatment. As to *in vitro* evaluations of anti-fungal medications, Wickware stated the following: "When evaluating a drug's potential against a particular infection, be aware that **microbial studies in culture are not a good indicator of clinical outcome...In general be wary of *in vitro* results, because they are not likely to be good indicators of *in vivo* susceptibility in a clinical context**" (Page 2 of printout).

There is no clear and convincing evidence that microorganisms such as bacteria are an appropriate model for the conditions of fungal infections and/or mutagenically caused conditions in humans or animals. In the absence of such evidence, and further in light of the State of the art, the examiner shall assume the microorganism model (*in-vitro* model) is insufficient for meaningful extrapolation.

Furthermore, Applicants have provided absolutely no data which would indicate that the composition of the Present invention would act beneficially in any inflammatory condition in a mammal or a human or even *in-vitro*. Absent such evidence, it would require a substantial inventive contribution from one of skill in the art to ascertain whether the extract of *Arisolochia taliscana* would work commensurate in scope with the Instantly claimed invention.

The worker of ordinary skill in the art would not be able to practice the invention as claimed, given the limited and incomplete description set forth in the Specification. It has been well established that disclosure in an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves." In re Gardner et al., 166 USPQ 138 (CCPA 1970).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 53-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 53-64 recite the term 'extract' from *Aristolochia taliscana*. The term 'extract' is considered indefinite in that it does not clearly define the meets and bounds of the term. There are numerous extractions which could be performed on *Aristolochia taliscana* which may provide for products (phytochemicals) which may not perform within the scope of the present invention. Limitation to the particular extraction method is suggested. For example, 'an effective amount of an organic solvent extract from Aristolochia taliscana...', or 'an effective amount of a benzene extract from Aristolochia taliscana.'

Claims 53-55 and 57 recite the term 'or one or more ...active compounds isolatable therefrom.' This statement is considered indefinite in that the composition defined by 'one or more' is not clearly delineated. It is not known exactly what compound or combinations of compounds would perform as beneficially as the crude extract of the Present invention, especially since all of the examples presented in the Instant specification (anti-fungal, anti-mutagenic) were performed with the crude extract. Clarification is necessary.

Claims 55 and 57 are indefinite in that they recite 'or one or more component compounds isolatable therefrom' and 'one or more antifungally active compounds isolatable therefrom' respectively. It is unclear which compounds the Claims are referring to, since there are many compounds defined in the Instant specification. Which individual compounds disclosed would

necessarily produce an equivalent effect in an individual suffering from a chronic inflammatory disease or a fungal infection? Furthermore, does the Instant specification provide such guidance which corresponds to the individual compounds? Correction is necessary.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 65-71 are rejected under 35 U.S.C. 102(b) as being anticipated by de la Parra (US 4,782,077). Claims 65-71 are drawn to a composition derived from the organic solvent extraction of Aristolochia species. Claims are further drawn to where the composition contains specific amounts of eupomatenoids and where the composition contains arisolactam.

de la Parra (US 4,782,077) disclosed a hexane/benzene extraction of *Aristolochia taliscana* root (Col.4, lines 61-68 and Col. 5, lines 1-9). Thus, the composition of Claims 65-71 was known at the time of the Instant disclosure. Where the claims recite eupomatanoids and/or arisolactam are merely inherent properties of an already known composition. Even though de la Parra was silent as to these inherent characteristics of the *Aristolochia taliscana* root extract:

In re Sussman, 141 F. 2d 267, 60 U.S.P.Q. 538 (CCPA 1944), the claims are rejected under 35 U.S.C. 102 (b) as well as 35 U.S.C. 112, first and second paragraph, "that **since the steps are the same, the results must inherently be the same** unless they are due to conditions not recited in the claims." In the particular case, Applicant(s) is (are) claiming an invention employing the **same process steps** but the product(s) is(are) **alleged to be different**. Applicant is required to recite the missing steps to form the alleged different product(s) in view of the above cited decision.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 54 is rejected under 35 U.S.C. 102(b) as being anticipated by Angeles et al. (1970).

Claim 54 is drawn to a method of treating a disease state mediated by mutagenesis comprising administration of an antimutagenic extract from Aristolochia species.

Angeles et al. (1970) disclosed that aristolochic acid, which was extracted from *Aristolochia tagala* showed anti-tumor activity in female white mice (Please see Chart II, Table 3 and pp. 519, Col.1).

Thus, the method of treating a disease state mediated by mutagenesis comprising administration of an antimutagenic extract from **Aristolochia species** was anticipated by Angeles et al.

Claims 53 and 55-64 are free of the art, however, were rejected under 35 U.S.C 112 1st paragraph (*supra*).

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Patricia Patten, whose telephone number is (703)308-1189. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jon P. Weber, Ph.D.
Primary Examiner